Distinguish, Remember and Adapt to Environments: A Strategy to Survive

Ganhui Lan[1], Yuhai Tu[2]

***Short Abstract* — Bacteria are capable to recognize and adapt to complex extra-cellular environments. In this work, we develop a model to understand how bacterial receptors process mixed signals that contain multiple chemical stimuli to maintain precise adaptation. The model takes into account effects of both local and global kinase activity when simulating methylation kinetics of individual receptor. Results show that methylation levels of different receptors reflect concentration of corresponding ligands that they bind with, which separates and stores stimuli compound information. We predict that local effect can enhance receptor sensitivity under any ambient chemical condition.**

***Keywords* — adaptation kinetics, bacterial chemotaxis, heterogeneous receptor cluster, signal processing.**

I. Background and Motivation

Tar (R_1) and Tsr (R_2) receptors are bacterial chemo-receptors binding with Aspartate (L_1) and Serine (L_2), respectively. They form hetero-trimers of homo-dimmers on bacterial membrane [1], and trimers aggregate at cell pole to form clusters through CheW/CheA proteins [2, 3]. In bacterial chemotaxis, ligand binds to receptors and changes CheA phosphorylation activity, which eventually regulates flagella motor switch. The subsequent sensory adaptation is carried out by receptor methylation. Receptors within a heterogeneous receptor cluster couple to each other and enhance the cell's chemotactic sensitivity [4].

The cooperative kinase activity was successfully modeled by the classical Monod-Wyman-Changeux (MWC) allosteric model [4]. However, because of the all-or-none assumption, MWC type model is blind to the difference between ligands and therefore insufficient in describing methylation kinetics with multiple stimuli. Here, we describe our effort in developing theory and models based on microscopic knowledge of the signaling pathway and existing experiments to elucidate several important questions: 1) How can bacteria tell the difference among different stimuli; 2) where and how are the information of the multiple ligands encoded; 3) How such information can be used to enhance sensitivity in complex environment with multiple cues.

IBM Thomas J. Watson Research Center. P. O. Box 218, Yorktown Heights, NY 10598.
[1]E-mail: glan@us.ibm.com
[2]Correspondence author. E-mail: yuhai@us.ibm.com

II. Model and Result

In this presented model, we propose dependence of methylation kinetics on local activity, and unlike MWC type model, we assume finite coupling strength between receptors. So each receptor undergoes its own adaptation kinetics instead of being dictated by the cluster. This model makes unique predictions about heterogeneous receptor cluster (i.e. R_1, R_2) adaptation kinetics when one type of ligand (i.e. L_1) is added.

A. Recovery state

After the initial drop in activity, methylation starts and activity of both receptors recovers. For R_1, activity and methylation increase monotonically: activity reaches its original level and methylation stays at higher value; nevertheless, for R_2, activity and methylation both over-shoots to higher values and then decreases to their original levels.

B. Steady state

When the system reaches steady state, methylation level of R_1 increases but that of R_2 remains original value. These result in unchanged activity levels for both types of receptors.

C. Sensitivity

We evaluate sensitivity of the receptor cluster under variant levels of L_1 and L_2. Our evaluation indicates that local effect tends to optimize both kinds of receptors to their most sensitive regime. In consequence, our proposed model obtains higher gain in chemo-sensing than MWC type model.

III. Conclusion

We developed a model for understanding how bacteria distinguish, remember and adapt to mixed stimuli. Predicts from our model, such as over-shooting behavior of the assisting receptor during recovery stage and higher sensitivity to mixed stimuli, can be verified by future experiments.

References

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